# World Trade Center Health Program Research Projects
# Eight Awarded Contracts
# September 30, 2011

**1. Title:** Pulmonary Function Abnormalities, Diastolic Dysfunction and World Trade Center Exposure - Implications for Diagnosis and Treatment
**Organization:** Mount Sinai School of Medicine
**Principal Investigator:** Mary Ann McLaughlin, M.D.

**Abstract:**
In response to the need to develop clinical research focused on investigating the important pathophysiologic mechanisms of disease following different degrees of exposure to the World Trade Center disaster, as well as to provide longitudinal data building on current knowledge, we aim to complete the following objectives:

Objective 1: To evaluate the persistent longitudinal effects of pulmonary function abnormalities (spirometry) and additionally demonstrate prevalence of impaired diffusing capacity of the lung for carbon monoxide (DLCO) in WTC responders.
Hypothesis: Intensity of exposure to acute inhaled particulates at Ground Zero will be an independent predictor of sustained pulmonary function abnormality (spirometry) and in addition, will predict impaired DLCO.

Objective 2: To determine the relationship between pulmonary function abnormalities (spirometry and DLCO) and cardiac dysfunction as measured by right ventricular (RV) diastolic dysfunction.
Hypothesis: Persistent pulmonary dysfunction predicts incidence of RV diastolic dysfunction.

Objective 3: To evaluate the association between levels of exposure to inhaled particulate matter on cardiac dysfunction as measured by LV diastolic function or evidence of subclinical atherosclerosis with high risk coronary calcium scores in WTC responders.
Hypothesis: Exposure to acute inhaled particulates independently predicts left ventricle (LV) and right ventricle (RV) dysfunction assessed by echocardiography and subclinical atherosclerosis as defined by high risk coronary calcium score.

Objective 4: To determine the risks of developing obstructive sleep apnea (OSA) in the WTC responder population, and to evaluate the effect of OSA on mediating diastolic dysfunction.
Hypothesis: Exposure to inhaled particulates increases risk of OSA, and ultimately cardiac diastolic dysfunction.

Objective 5: To demonstrate specific mediators and pathways that link effects of inhaled particulate matter to microvascular and cardiovascular disease. This objective will be explored using measurements of vascular reactivity (peripheral arterial tonometry) and serum inflammatory and hemostatic markers from blood stored at the initial monitoring visit, as well as current blood samples.
Hypothesis: Inhaled particulate matter contributes to poor endothelial function both directly and indirectly through inflammation and altered hemostasis. Degree of inflammation detected through laboratory evaluation at time of initial visit will predict persistent effects on

vasculature, as demonstrated by cardiac diastolic dysfunction and impaired vascular reactivity.

**2. Title:** Burden of Mental-Physical Comorbidity in World Trade Center Responders
**Organization:** State University of New York, Stony Brook
**Principal Investigators:** Evelyn Bromet, Ph.D. and Roman Kotov, Ph.D. from the Department of Psychiatry; Benjamin Luft, M.D. from the Department of Medicine

**Abstract:**
The ultimate objective of the proposed study is to learn about the impact of mental-physical comorbidity, mechanisms that maintain it, and intervention strategies that can address it. We propose to study responders participating in the WTC-MMTP. Of the entire cohort, approximately 16,000 completed the first two monitoring visits, about two years apart. These longitudinal data will allow us to evaluate potential mechanisms underlying the links between mental and physical disorders. We also propose to conduct telephone interviews with a subsample of 5,000 responders to obtain data on DSM-IV PTSD and key outcomes, including quality of life, role functioning, and health risk perceptions. Furthermore, some of the WTC-MMTP sites (i.e., Long Island) provide integrated mental and physical health services, while other sites refer patients to mental health specialists off site. This natural experiment will allow us to investigate potential benefits of the integrated care approach.

Aim 1: To test mechanisms thought to be responsible for the comorbidity between psychiatric and medical sequelae of WTC exposures. We will examine PTSD symptoms as well as medical problems (lower respiratory symptoms, asthma, abnormal lung function, GERD, hypertension) at the first and second monitoring visits. Thus, we will investigate both new and persistent conditions detected at follow-up. We will evaluate several questions regarding the nature of mental-physical comorbidity, such as whether PTSD contributes to development of medical problems, and whether medical problems help to maintain PTSD.

Aim 2: To evaluate the impact of PTSD-medical comorbidity on quality of life, functioning, and health risk perceptions of WTC responders. The WTC-MMTP did not collect systematic data on DSM-IV PTSD diagnosis, or adequate measures of quality of life and role functioning, which are significantly affected by comorbidity (Eaton et al. 2008; Merikangas et al. 2007; Scott et al. 2009; Yohannes et al. 2010), or health risk perceptions, which are unique consequences of toxic exposures (Havenaar, Cwikel & Bromet 2002). We thus propose to conduct computer-assisted telephone interviews using state-of-the-art measures with a representative subsample (N = 5,000) of the WTC-MMTP cohort to obtain these data allowing us to compare outcomes of patients with comorbid conditions to those with medical disorders or PTSD alone.

Aim 3: To compare the benefits of integrated care strategy to a conventional gateway model in treating responders with comorbid conditions. We will compare outcomes of patients monitored at the Long Island site to that of other WTC-MMTP sites, controlling for demographic and illness characteristics at the first visit. In the full Visit 2 cohort, the outcomes will include probable PTSD and medical conditions at Visit 2. In the telephone subsample, outcomes will be extended to quality of life, role functioning, and health risk perceptions. We expect participants receiving integrated care to show greater improvement, especially those with comorbid mental and physical problems. The findings, particularly if confirmed across multiple outcomes, will provide crucial evidence about service delivery practices that may be most beneficial for this population.

**3. Title:** Evaluation of Distal Airway Injury Following Exposure to World Trade Center Dust
**Organization:** New York University School of Medicine
**Principal Investigator:** Kenneth I. Berger, M.D.

**Abstract:**
To enhance characterization of airway injury in subjects enrolled in the Bellevue Hospital WTC EHC by evaluating spirometry and assessment of distal airway function.
Hypothesis: Airway dysfunction undetected by spirometry, and potentially in the distal airways is an important component of lung injury in subjects following exposure to WTC dust. To test this hypothesis, analysis of cross sectional data obtained in 3000 subjects for both spirometry and oscillometry will be analyzed.

- To summarize spirometry assessment of lung function in the population of patients enrolled in the Bellevue Hospital WTC Environmental Health Center
- To summarize results from oscillometric assessment of lung function in the population of patients enrolled in the Bellevue Hospital WTC Environmental Health Center
- To determine the benefit of performing IOS in addition to spirometry to detect lung injury in the distal airways by analyzing the relationship of IOS abnormalities to spirometry results.
- To determine the relationship of IOS abnormalities to type and degree of WTC dust/fume exposure as well as presence and persistence of lower respiratory symptoms.
- To evaluate for reversibility by analyzing the responsiveness of IOS abnormalities to administration of short acting b-agonist.

To determine the relationship between development of distal airway dysfunction and simultaneous development of respiratory symptoms during induced bronchoconstriction in subjects enrolled in the Bellevue Hospital WTC Environmental Health Center.
Hypothesis: Distal airway dysfunction may be associated with onset of methacholine-induced symptoms even in subjects without significant spirometric response providing clinical relevance to the oscillometric abnormalities. To test this hypothesis, analysis of data obtained in subjects during methacholine challenge testing will be analyzed.

- To evaluate changes in spirometric and oscillometric indices of airway function in response to inhaled methacholine.
- To evaluate the association between presence of bronchial hyper-reactivity to both WTC exposure and presence of lower respiratory symptoms.
- To determine concordance and disparity between spirometric and oscillometric responses to inhaled methacholine.
- To determine the relationship of symptom onset to changes in spirometry and IOS during methacholine challenge testing.

To determine longitudinal lung function as assessed by spirometry and oscillometry in a diverse population exposed to WTC dust while undergoing standardized evaluation and therapy.
Hypothesis: Longitudinal assessment of lung function (spirometry and IOS) in subjects enrolled in the Bellevue Hospital WTC EHC will vary based on the initial abnormality and subsequent therapy. To test this hypothesis, analysis of longitudinal data will be analyzed in subjects who return for follow-up evaluation and monitoring.

- To determine relationship between evolution of these indices of lung function to baseline pattern of dysfunction.
- To determine the relationship between evolution of lung function to type of exposure and persistence of lower respiratory symptoms.
- To determine the relationship between chronic response lung function to therapy as compared to degree of acute responsiveness at baseline (as tested with short acting b-agonist).
- To determine the differential effects of differing medical regimens on the evolution of lung function.

**4. Title:** Cohort Study of Incident Cancer in the FDNY Responder Population
**Organization:** Fire Department of New York
**Principal Investigator:** David Prezant, M.D.

**Abstract:**
The main objective of this three-year research project is to analyze the cohorts of FDNY firefighters and EMS workers, both WTC-exposed and non-WTC exposed in order to compare cancer incidence by WTC-exposure status during the early post-9/11 years. To achieve this objective, we intend to conduct longitudinal surveillance of cancer diagnoses in WTC-exposed and non-WTC-exposed individuals through 2008 and later, as data become available. We have already completed analyses in an FDNY firefighter cohort on cancer incidence rates 7 years post-9/11. We will continue to add follow-up observational years to the firefighter cohort, conduct similar analyses in FDNY EMS workers and then compare the cancer burden between these two cohorts. These populations are treated as two distinct groups of workers because of previously described demographic and exposure differences.

The research in this proposal will benefit the WTC program and the cohort it serves. If cancer rates are increased, then a screening and treatment program can be tailored to the specific-sites or organs that are affected and the cohort can receive targeted education on strategies to prevent and find earlier expected future cancers. In contrast, if these analyses show that cancer is not increased in the two different groups (Fire and EMS) with well documented but different exposures and similar access to healthcare (e.g. similar case surveillance issues), then this information can be communicated to the cohort in a responsible fashion identifying that longer term studies are still needed but that until the evidence to the contrary, limited healthcare dollars should be directed otherwise.

**5**. **Title:** Trajectories of Psychological Risk and Resilience in World Trade Center Responders
**Organization:** Mount Sinai School of Medicine
**Principal Investigator:** Adriana Feder, M.D.

**Abstract:**
The objectives of the proposed study are to (1) characterize longitudinal trajectories of WTC-related PTSD and depressive symptoms in WTC responders; (2) examine specific risk and protective determinants of these trajectories; and (3) identify personal and psychosocial factors associated with resilience and recovery trajectories, with the ultimate goal of maximizing preparedness and improving mental health outcomes in disaster responders. We propose to make use of the unique dataset collected prospectively at the WTC-MMTP, beginning in 2002, to study longitudinal trajectories of WTC-related PTSD and depressive symptoms in 12,000 cohort members who completed three monitoring visits at the WTC-MMTP, each approximately two years apart. We then aim to investigate the association between longitudinal trajectories of PTSD and depressive symptoms, and personal characteristics (e.g., age, gender, physical health); specific WTC exposures (e.g., handling human remains; loss of family, friends or colleagues during 9111; specific working conditions such as hours and intensity of work at Ground Zero, and sleeping at the WTC site; availability of family and work support); and post-WTC events (e.g., stressful life events and degree of social support). Finally, we propose to contact a sample of 6,000 workers to conduct a survey that will provide vital new information on detailed personal and psychosocial factors that distinguish WTC responders in the hypothesized resilience and recovery trajectories from those with symptom persistence and impaired functioning (i.e., chronic or delayed dysfunction). Characterization of this comprehensive set of risk and protective factors is essential to informing the development of empirically-based prevention and treatment intervention strategies for rescue and recovery workers.

**6. Title:** Enhanced Smoking Cessation Intervention for World Trade Center Responders
**Organization:** Research Foundation of the State University of New York
**Principal Investigator:** Evelyn Bromet, Ph.D.

**Abstract:**
The objective of this study is to adapt and test an enhanced smoking cessation treatment for WTC responders burdened with PTSD symptoms. We will recruit 100 smokers who have significant PTSD symptoms from the population monitored at the Long Island site of the WTCMMTP. We will over-sample patients with lower respiratory illness to ensure that at least two-thirds have these symptoms. We will randomly assign participants to either: (1) standard smoking cessation or (2) enhanced smoking cessation (nicotine replacement therapy will be administered to both groups). Outcomes will be assessed at five follow-ups, the last of which will be 6 months after the quit date. Our specific aims are:

Aim 1: To compare, in a randomized clinical trial, the effect of enhanced treatment vs. standard treatment on the following smoking cessation outcomes:

A. Short- and long-term point prevalence abstinence. We expect it to be higher in the enhanced treatment condition.

B. Time to first smoking lapse and time to smoking relapse. We expect mean time to first lapse and to relapse to be greater in the enhanced treatment condition.

Aim 2: To evaluate the effect of enhanced compared to standard treatment on PTSD symptoms. We predict that PTSD symptoms will decline more in the enhanced treatment condition both in the short- and long-term.

Aim 3: To compare the benefits of enhanced vs. standard treatment for pulmonary health. We hypothesize that at the 6-month follow-up, reduction in lower respiratory symptoms will be greater in the enhanced treatment condition. In secondary analyses, we will evaluate whether improved pulmonary health is due to reduction in smoking, PTSD symptoms, or both.

This project will produce a powerful new intervention for a difficult to treat group of WTC responders (smokers with PTSD symptoms). We expect that this treatment will help to reduce both smoking and PTSD morbidity, resulting in improved pulmonary health. If this study confirms our predictions, it will be possible to implement enhanced smoking cessation at other WTC-MMTP sites easily and inexpensively. Our next step will be a large, multi-site effectiveness study of this treatment. Importantly, this intervention also will be directly applicable to veterans and responders to other disasters who suffer from nicotine addiction and PTSD symptoms. Furthermore, the proposed study will shed light on the nature of comorbidity between PTSD and respiratory symptoms.

**7. Title:** Cancer Among WTC Responders: Enhanced Surveillance, Exposure, Assessment, and Cancer Specific Risk
**Organization:** Mount Sinai School of Medicine
**Principal Investigator:** Paola Boffetta, M.D.

**Abstract:**
The overarching objective of the project is to define whether or not WTC responders included in the WTCHP experienced an increased risk of cancer and whether or not such increase can be associated with WTC-related exposures. The specific aims of the project are:

Aim 1: To identify and confirm all cases of cancer occurring among WTC responders included in WTCHP, using multiple sources of information and developing algorithms for confirmation of cancer diagnosis.

Aim 2: To develop and apply an exposure assessment procedure to estimate Exposure Ranking Indices (ERIs) for selected known and suspected carcinogens for all WTCHP responders, and to conduct a systematic analysis of exposure-cancer associations, based on ERIs.

Aim 3: To conduct in-depth analyses of exposure-cancer associations.
MSSM:

**8. Title:** WTC-HEART: Cardiovascular Health Impact and Prediction of Incident (primary and subsequent) Cardiovascular Events Among WTC Responders
**Organization:** Research Foundation of CUNY-Queens College
**Principal Investigator:** Steven Markowitz, M.D.

**Abstract:**
The proposed study will determine whether:

1) The FHS risk score, as expected, underestimates the WTC cohort's CHD risk for primary and subsequent cardiac events;

2) A specific WTC risk score needs to be established to identify the high-risk responders and guide cardiovascular prevention;

3) WTC workers are at higher CVD risk than other New York residents who were not directly exposed to the air pollution and mental stress at Ground Zero. For the third objective, the follow-up of the WTC responders aged 55 years and over will be compared to that of the concurrent INVEST cohort, comprising NYC residents of Washington Heights, that is, a neighborhood located at the extreme opposite of Manhattan, in which habitants are likely not to have been exposed to a large extent to WTC-related air pollution and stress.

It will deliver a practical clinical procedure for the management of CVD risk specifically developed in the WTC responder population.